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EXAMINER
HAYES, ROBERT CLINTON

ART UNIT	PAPER NUMBER
1647	9

DATE MAILED: 01/28/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/619,198	Yan et al
Examiner	**Art Unit**
Robert C. Hayes, Ph.D.	1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Nov 6, 2001* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above, claim(s) *2, 4, and 14-21* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1, 3, and 5-13* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☒ Claims *1-21* are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 5

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

DETAILED ACTION

Election/Restriction

1. Applicant's election with traverse of Group I (claims 1-4, 5a & 6-13), as it relates to the polypeptide of SEQ ID NO:7, in Paper No. 8 is acknowledged. The traversal is on the ground(s) that "the polypeptides of the Group IV and V constitute fragments of the polypeptides of Group I". The Examiner agrees, and therefore, rejoins these groups (i.e., as it relates to SEQ ID NO:7), as well as the variants of the polypeptide of SEQ ID NO:7 in Groups II-III (i.e., claims 1, 3 & 5-13). Applicants then argue that "the polypeptides of SEQ ID NOs: 1-10 are not entirely unrelated sequences"... and therefore, "there would be no undue hardship on the office in preforming a search with respect to the polypeptides of SEQ ID NOs: 1-10". However, this is not found persuasive because each of these sequences are unique, as exemplified by their unique SEQ ID NOs, in which the non-coextensiveness of the search and examination for each group would constitute an undue burden on the examiner to search and consider all the separable groups with their recognized divergent subject matter, as illustrated in Table 1 on page 7 of the specification. The requirement is still deemed proper and is therefore made FINAL.

Claims 2, 4 & 14-21 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to non-elected inventions, the requirement having been traversed in Paper No. 4.

This application contains claims 2, 4 & 14-21 drawn to an invention nonelected with traverse in Paper No. 8. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Drawings

2. The drawings are objected to as failing to comply with 37 CFR 1.84(p)(5) because they include the following reference sign(s) not mentioned in the description: It is unknown what the number values represent in Figures 2-3, in that no units, etc. are listed or described. Figure 1 also appears to be incorrectly listed as Figure 3 on page 6 of the specification. Correction is required.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3 & 5-13 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

No written description is provided in the instant specification as to what structurally constitutes the broader generic polypeptide sequences that *comprise* unknown and undescribed

sequences, that are fused to unknown or undescribed heterologous polypeptide (i.e., as it relates to claim 6) or what constitutes allelic variants of the polypeptide of SEQ ID NO:7 from rat or any different species (i.e., as it relates to claims 3 & 5), in that no sequences for these different molecules are described that constitute an open reading frame; nor can they be reasonably visualized by one skilled in the art. In contrast, the sole unique species of a rat VGF polypeptide of SEQ ID NO:7 is described, versus that recited on page 8 of specification where alternatively "polypeptide[s] from another species" are claimed to be part of the invention.

Therefore, because one skilled in the art cannot reasonably visualize or predict what critical encoded amino acid residues would structurally characterize the genus of VGF polypeptides encompassed by the current claims, because it is unknown and not described what structurally constitutes such VGF polypeptides from any different species, or what constitutes any functional fragments thereof when none are described, the written description requirements under 35 U.S.C. 112, first paragraph are not met.

Applicants are directed toward the Revised Interim Utility and Written Description Guidelines, Federal Register, Vol.64, No.244, pages 71427-71440, Tuesday December 21, 1999.

4. Claims 1, 3 & 5-13 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polypeptide consisting of the sequence set forth in SEQ ID NO:7 that increase body weight, does not reasonably provide enablement for randomly mutated/modified polypeptides with no definable or known function. The specification does not

enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The name "VGF polypeptide" (as it relates to how it is defined on pages 6 and 8 of the specification) does not sufficiently characterize and enable the full scope of the polypeptides encompassed by the current claim language, because the inclusion of any "fragments, orthologs, variants, derivatives", "substitutions..., deletions..., and/or additions", or any biological functional equivalent, within the definition of VGF polypeptides sets forth little structural and functional characteristics. Importantly, the specification does not teach which particular amino acids are critical for any VGF protein's function, nor how to distinguish any random fragment, conservatively substituted, insertion, deletion, C- and/or N-terminal truncation of the instant invention from any different VGF-related protein molecule that possesses none of the desired functions of the instant invention, if later defined. Therefore, any such broadly claimed polypeptides without recited and definable functional characteristics would be expected by the skilled artisan to encode inactive proteins. For example, Rudinger states on page 3 that "it is impossible to attach a unique significance to any residue in a sequence. A given amino acid will not by any means have the same significance in different peptide sequences, or even in different positions of the same sequence". Rudinger further states on page 6 that "the significance of particular amino acid sequences for different aspects of biological activity cannot be predicted *a priori* but must be determined from case to case by painstaking experimental study". Therefore, the lack of guidance provided in the specification as to what minimal structural requirements are

necessary for any VGF function would prevent the skilled artisan from determining whether any modification or mutation to the single disclosed rat VGF molecule of the instant invention could be made which retains the desired function of the instant invention, because any random mutation or modification manifested within a VGF protein would be predicted to adversely alter its biologically active 3-dimensional conformation, without requiring undue experimentation to determine otherwise.

Taking this point one step further, because the specification provides little guidance as to what constitutes the metes and bounds of an otherwise undefinable "activity of the polypeptide as set forth in... SEQ ID NO:7" (i.e., as it relates to claims 3 & 5-13), one of ordinary skill in the art would not know how to make and use any variant fragment, derivative, insertion (i.e., including conservatively substituted), deletion, C- and/or N-terminal truncation of the instant invention comprising "pharmaceutically" acceptable formulations (i.e., as it relates to claims 8-9), because no assay nor therapeutic use to determine what constitutes such an undefinable "activity of the polypeptide as set forth in... SEQ ID NO:7" is described within the specification, nor claimed; thereby, requiring undue experimentation to determine such. In other words, Figure 1 appears to represent the sole described use for the instant invention, which involves weight gain following administration of VGF polypeptides, which by itself does not define the metes and bounds encompassed by the broader recitation, "activity of the polypeptide as set forth in... SEQ ID NO:7".

5. Claims 3 & 5-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The metes and bounds of what constitutes "has the activity of the polypeptide as set forth in any of SEQ ID NO:..." is not recited and unknown.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3, 5-6 & 8-11 are rejected under 35 U.S.C. 102(b) as being anticipated by Salton et al. (1991).

Salton et al. teach the sequence of rat VGF/NGF33.1 which "comprises the amino acid sequence as set forth in... SEQ ID NO:7" (i.e., pg. 993, Fig. 1; as it relates to claim 1), which also meets the limitations of being a "fusion polypeptide comprising the polypeptide of... SEQ ID NO:7", because additional heterologous amino acid residues sequences are fused to the polypeptide of SEQ ID NO:7 (i.e., as it relates to claim 6). A fragment of SEQ ID NO:7 common between VGF and NGF33.1 is also indicated by Salton that consists of positions 317-341 (i.e., Fig. 1; as it relates to claim 3), which comprises "at least one amino acid deletion" (i.e.,

as it relates to claim 5c & e), as well as a C-terminal truncation of SEQ ID NO:7 (i.e., as it relates to claim 5d & e). In that Salton's polypeptides further contain at least one amino acid insertion to that set forth in SEQ ID NO:7, the limitations of claims 5b & 5e are anticipated. In that any of these modifications to the amino acid sequence depicted as SEQ ID NO:7 as disclosed by Salton et al. constitute a derivative polypeptide, by definition, when compared to SEQ ID NO:7, and because a "polymer" of water soluble amino acid residues are covalently attached to SEQ ID NO:7, etc., the limitations of claims 10 & 11 are met. Lastly, any "activity of the polypeptide as set forth in... SEQ ID NO:7" inherently is possessed by the above recited molecules because they structurally meet the limitations of that claimed; absent evidence to the contrary. Note, that because water is a pharmaceutically acceptable formulation agent/carrier/adjuvant/solubilizer/ stabilize that comprises Salton's polypeptides, the limitations of claims 8-9 are also met.

7. Claims 3, 5-6 & 8-11 are rejected under 35 U.S.C. 102(b) as being anticipated by Possenti et al. (1989).

Possenti et al teach the sequence of rat VGF8a which "comprises" as a fusion protein (i.e., as it relates to claim 6) a fragment of the amino acid sequence as set forth in... SEQ ID NO:7" (i.e., from amino acid residues 316-340; pg. 2218, Fig. 1; as it relates to claim 3) which, therefore, by definition is also a "derivative" of the polypeptide of SEQ ID NO:7 (i.e., as it relates to claim 10), since additional sequences are inserted in this N- and C-terminal truncated/deleted fragment of SEQ ID NO:7 (i.e., as it relates to claims 5b, c, d & e). In that a

"polymer" of additional water soluble amino acid residues are covalently attached to this fragment of SEQ ID NO:7, the limitations of claim 11 are met. Note that lacZ fusion proteins comprising heterologous amino acid sequences fused to the fragment polypeptide of SEQ ID NO:7 for the production of polyclonal antibodies are also disclosed by Possenti et al. (i.e., Fig.1; as it relates to claims 5b, 5e, 6, 10-11). Note that any "activity of the polypeptide as set forth in... SEQ ID NO:7" inherently is possessed by the above recited molecules because they structurally meet the limitations of that claimed; absent evidence to the contrary. Note further that because water is a pharmaceutically acceptable formulation agent/carrier/adjuvant/solubilizer/ stabilize that comprises Possenti's polypeptides, the limitations of claims 8-9 are also met.

8. Claims 5-6 & 10-11 are rejected under 35 U.S.C. 102(b) as being anticipated by Canu et al. (IDS Ref #1).

Canu et al. teach the sequence of human and rat VGF, in which Canu's rat VGF polypeptide "comprises the amino acid sequence as set forth in... SEQ ID NO:7" with the conservative substitution of an alanine for a glycine (i.e., pg. 444, Fig. 1; as it relates to claims 5a & e) which, therefore, is a fusion polypeptide containing additional heterologous amino acid sequences (i.e., as it relates to claim 6), and which by definition is also a "derivative" of SEQ ID NO:7 (i.e., as it relates to claim 10). In that the human sequence contains at least one amino acid insertion (e.g., position #344), the limitations of claims 5b & 5e are met. Note that the dibasic site boundaries of the human variant peptide of SEQ ID NO:7 are further indicted in

Figure 1, which are proteolytic sites for "prohormone convertases" (pg. 444, 1st column; as it relates to claim 5b & e). In that a "polymer" of additional water soluble amino acid residues are covalently attached to Canu's conservatively substituted polypeptide, the limitations of claim 11 are met. Lastly, note that any "activity of the polypeptide as set forth in... SEQ ID NO:7" inherently is possessed by the above recited molecules because they structurally meet the limitations of that claimed; absent evidence to the contrary.

Conclusion

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Robert Hayes whose telephone number is (703) 305-3132. The examiner can normally be reached on Monday through Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Robert C. Hayes, Ph.D.
January 22, 2002

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